CHAPTER 33
FUNDAMENTAL PRINCIPLES OF RADIOBIOLOGY

Principal Aim of the Study of Radiobiology
- To understand radiation dose-response relationships

Dose-Response Relationship
- A mathematical & graphic function that relates radiation dose to observed response

Jean Bergonie & Louis Tribondeau (1906)
- Theorized & observed that radiosensitivity was a function of metabolic state of tissue being irradiated

LAW OF BERGONIE & TRIBONDEAU
- Stem cells are radiosensitive; Mature cells are radioresistant
- Younger tissues and organs are radiosensitive
- Tissues with high metabolic activity are radiosensitive
- A high proliferation rate for cells & a high growth rate for tissues result in increased radiosensitivity

Physical Factors That Affect Radiosensitivity
- Linear Energy Transfer (LET), Relative Biologic Effectiveness (RBE), Protaction & Fractionation

Linear Energy Transfer (LET)
- A measure of the rate at which energy is transferred from ionizing radiation to soft tissue
- *Another Method of:*
  - Expressing radiation quality
  - Determining the value of the radiation weighting factor (W_R)
    - Used in radiation protection
- *Expressed in:* keV/μm
- *Diagnostic X-rays:* 3 keV/μm
- *As LET Increases:*
  - Increases the ability to produce biologic damage
  - Increases the probability of interaction with the target molecule

Radiation Weighting Factor (W_R)
- Factor used in radiation protection that accounts for differences in biologic effectiveness between different radiations
- *Former Name:* quality factor

Relative Biologic Effectiveness (RBE)
- Ratio of the dose of standard radiation necessary to produce a given effect to the dose of test radiation needed for the same effect
- *Formula:*

$$\text{RBE} = \frac{\text{Dose of standard radiation necessary to produce a given effect}}{\text{Dose of test radiation necessary to produce the same effect}}$$

Orthovoltage X-rays
- The standard radiation by convention
- *Range:* 200-250 kVp
- It was used in radiation oncology

The RBE of diagnostic x-rays is 1!

LET & RBE OF VARIOUS RADIATION DOSES

TYPE OF RADIATION	LET (keV/μm)	RBE
25 MV x-rays	0.2	0.8
60Co gamma rays	0.3	0.9
1 MeV electrons	0.3	0.9
Diagnostic x-rays	3.0	1.0
10 MeV protons	4.0	5.0
Fast neutrons	50.0	10
5 MeV alpha particles	100.0	20
Heavy nuclei	1000.0	30

Protraction
- The dose is delivered continuously but at a lower dose rate

Fractionation
- The dose is delivered at the same dose in equal portions at regular intervals
- It reduces the effect

- *Rationale:* cells undergo repair & recovery between doses

Dose protraction & fractionations cause less effect because time is allowed for intracellular repair & tissue recovery!

Biologic Factors That Affect Radiosensitivity

- Oxygen Effect, Age, Recovery, Chemical Agents & Hormesis

Oxygen Effect

- *Oxygenated/Aerobic State:* tissue is more sensitive to radiation than *anoxic* & *hypoxic*

Oxygen Enhancement Ratio (OER)

- Ratio of the dose necessary to produce a given effect under anoxic conditions to the dose necessary to produce the same effect under aerobic conditions
- *Formula:*

$$\text{OER} = \frac{\text{Dose necessary under anoxic conditions to produce a given effect}}{\text{Dose necessary under aerobic conditions to produce the same effect}}$$

- LET dependent
- *Low LET:* higher OER

Hyperbaric/High Pressure Oxygen

- It has been used in radiation oncology
  - *Purpose:* to enhance the radiosensitivity of nodular & avascular tumors

Diagnostic x-rays imaging is performed under conditions of full oxygenation!

Age

- *Before Birth:* most radiosensitive
- *After Birth:* radiosensitivity decreases
- *Maturiry:* most radioresistant
- *Old Age:* somewhat more radiosensitive

Recovery

- Intracellular Repair + Repopulation

Interphase Death

- It occurs when the cell dies before replicating

Intracellular Repair

- It is due to a repair mechanism inherent in the biochemistry of the cell

Repopulation

- Replication by surviving cells

The combined processes of intracellular repair & repopulation contribute to recovery from radiation damage!

Chemical Agents

- *Radiosensitizers:* agents that enhance the effect of radiation
  - *Examples:*
    - Halogenated pyrimidines
    - Methotrexate
    - Actinomycin D
    - Hydroxyurea
    - Vitamin K
- *Radioprotectors:* agents that reduces the effect of radiation
  - Not found human application
    - *Rationale:* it must be administered at toxic levels
  - *Examples:*
    - Cysteine
    - Cysteamine

Hormesis

- A little bit of radiation is good for us
  - *Rationale:* it stimulates hormonal & immune responses to other toxic environmental agents

RADIATION DOSE-RESPONSE RELATIONSHIPS

Radiation Dose-Response Relationship

- A mathematical relationship between various radiation dose levels & magnitude if the observed response

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Two Important Applications in Radiology
- It is used to design therapeutic treatment routines for patient with cancer
- It revealed provide the basis for radiation control activities

Two Types of Radiation Responses
- Deterministic/Nonstochastic
  - It follows a high-dose exposure
  - Early radiation response
  - *Example:* skin burn
- Stochastic
  - It follows a low-dose exposure
  - Late radiation response
  - *Examples:* cancer, leukemia & genetic effects

Two Characteristic of Dose-Response Relationship
- Linear or Nonlinear
- Threshold or Nonthreshold

Threshold Dose
- The level below which there is no response

Linear Dose-Response Relationship
- The response is directly proportionate to the dose
- *Linear Nonthreshold Type:* intersects at zero or below
  - It is used in establishing radiation protection guidelines for diagnostic imaging
- *Linear Threshold Type:* intercept the dose axis at some value greater than zero

Radiation-induced cancer, leukemia, & genetic effects follow a linear-nonthreshold dose-response relationship!

Nonlinear Dose-Response Relationship
- The response is not directly proportional to the dose
- *Nonlinear Nonthreshold:* large response results from a very small radiation dose
- *Nonlinear Threshold Type:* below the threshold, no response is measured

S-Type/Sigmoid-Type
- *Example:* skin effects resulting from high dose fluoroscopy

Diagnostic radiology is concerned almost exclusively with the late effects of radiation exposure & therefore, with linear, nonthreshold dose-response relationships!

CONSTRUCTING A DOSE-RESPONSE RELATIONSHIP

A dose-response relation is produced when high-dose experimental data are extrapolated to low doses!

Extrapolation
- Estimation of value beyond the range of known values
- *Results in:* linear, nonthreshold dose-response relationship